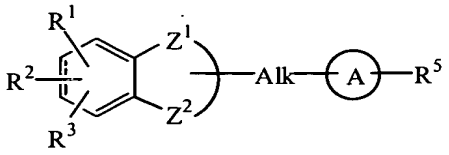
Claims

1. A compound of formula (I)



(I),

a stereochemically isomeric form thereof, an *N*-oxide form thereof, a pharmaceutically acceptable acid addition salt thereof, or a quaternary ammonium salt thereof, wherein

Alk is C_{1-4}alkylcarbonyl, C_{1-4}alkylcarbonylC_{1-4}alkyl, carbonyl, carbonylC_{1-4}alkyl, or C_{1-6}alkanediyl optionally substituted with hydroxy, halo, amino, hydroxyC_{1-4}alkyl, C_{1-4}alkyloxy, C_{1-4}alkyloxyC_{1-4}alkyl, C_{1-4}alkylcarbonyloxy, C_{1-4}alkylcarbonyloxyC_{1-4}alkyloxycarbonyloxy, or C_{3-6}cycloalkylcarbonyloxyC_{1-4}alkyloxycarbonyloxy;

$-Z^1-Z^2-$ is a bivalent radical of formula

$-O-CH(R^4)-CH_2-$ (a-1),
$-O-CH(R^4)-CH_2-O-$ (a-2),
$-O-CH(R^4)-CH_2-S-$ (a-3),
$-O-CH(R^4)-CH_2-CH_2-$ (a-4),
$-O-CH(R^4)-CH_2-CH_2-CH_2-$ (a-5),
$-O-C(R^4)=CH-$ (a-6),
$-O-C(R^4)=CH-CH_2-$ (a-7),
$-O-C(R^4)=CH-CH_2-CH_2-$ (a-8), or
$-O-CH(R^4)-CH=CH-$ (a-9),

wherein optionally one or two hydrogen atoms on the same or a different carbon atom may be replaced by hydroxy;

R^1, R^2 and R^3 are each independently selected from hydrogen, C_{1-6}alkyl, C_{3-6}alkenyl, C_{1-6}alkyloxy, trihalomethyl, trihalomethoxy, halo, hydroxy, cyano, nitro, amino, C_{1-6}alkylcarbonylamino, C_{1-6}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxy, aminocarbonyl, mono- or di(C_{1-6}alkyl)aminocarbonyl, aminoC_{1-6}alkyl, mono- or di(C_{1-6}alkyl)aminoC_{1-6}alkyl, C_{1-4}alkylcarbonyloxy-C_{1-4}alkyloxycarbonyloxy, or C_{3-6}cycloalkylcarbonyloxyC_{1-4}alkyloxy-carbonyloxy; or

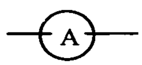
when R^1 and R^2 are on adjacent carbon atoms, R^1 and R^2 taken together may form a bivalent radical of formula

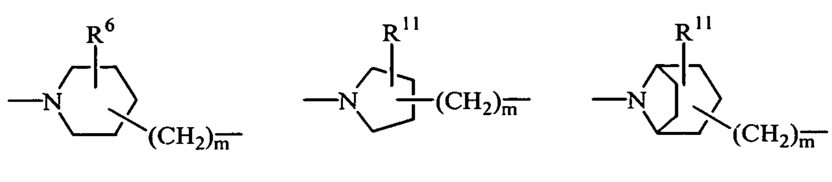
$-CH_2-CH_2-CH_2-$ (b-1), $-O-CH_2-CH_2-$ (b-6),

$-CH_2-CH_2-CH_2-CH_2-$	(b-2),	$-O-CH_2-CH_2-O-$	(b-7),
$-CH_2-CH_2-CH_2-CH_2-CH_2-$	(b-3),	$-O-CH_2-CH_2-CH_2-$	(b-8),
$-CH=CH-CH=CH-$	(b-4),	$-O-CH_2-CH_2-CH_2-CH_2-$	(b-9),
$-O-CH_2-O-$	(b-5),		

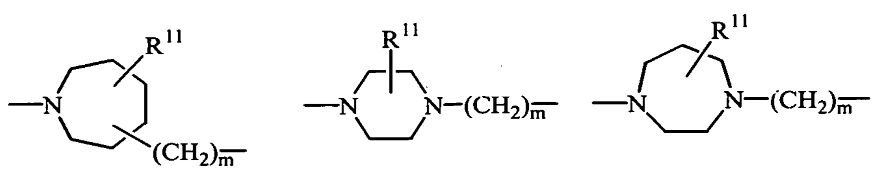
wherein optionally one or two hydrogen atoms on the same or a different carbon atom may be replaced by hydroxy, C_{1-4}alkyl or CH_2OH;

R^4 is hydrogen, C_{1-6}alkyl, phenylmethyl, hydroxyC_{1-4}alkyl, C_{1-4}alkyloxyC_{1-4}alkyl, C_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxyC_{1-4}alkyloxycarbonyl, C_{3-6}cycloalkylcarbonyloxyC_{1-4}alkyloxycarbonyloxy, or a direct bond when the bivalent radical $-Z^1-Z^2-$ is of formula (a-6), (a-7) or (a-8);

 is a bivalent radical of formula



(c-1) (c-2) (c-3)



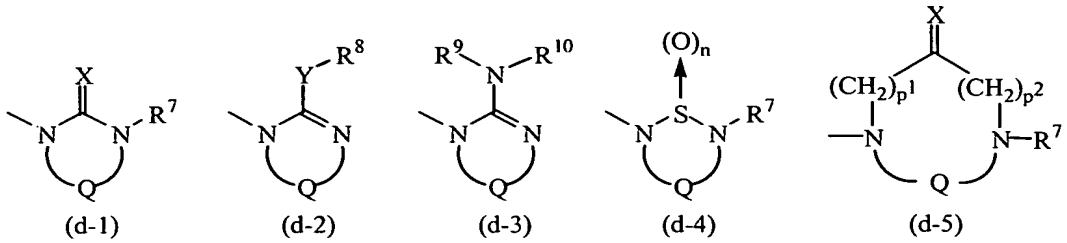
(c-4) (c-5) (c-6)

wherein m is 0 or 1;

R^6 is C_{1-4}alkyl, halo, hydroxy, hydroxyC_{1-4}alkyl, C_{1-4}alkyloxy, aminoC_{1-4}alkyl,C_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxyC_{1-4}alkyloxycarbonyl, or C_{3-6}cycloalkylcarbonyloxyC_{1-4}alkyloxycarbonyloxy;

R^{11} is hydrogen, C_{1-4}alkyl, halo, hydroxy, hydroxyC_{1-4}alkyl, C_{1-4}alkyloxy, aminoC_{1-4}alkyl, C_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxyC_{1-4}alkyloxycarbonyl, or C_{3-6}cycloalkylcarbonyloxyC_{1-4}alkyloxycarbonyloxy;

R^5 is a radical of formula



(d-1) (d-2) (d-3) (d-4) (d-5)

wherein n is 1 or 2;

p^1 is 0, and p^2 is 1 or 2; p^1 is 1 or 2, and p^2 is 0;

X is oxygen, sulfur, NR^9 or $CHNO_2$;

Y is oxygen or sulfur;

R^7 is hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, phenyl or phenylmethyl;

R^8 is C_{1-6}alkyl, C_{3-6}cycloalkyl, phenyl or phenylmethyl;

R^9 is cyano, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{1-6}alkyloxycarbonyl or aminocarbonyl;

R^{10} is hydrogen or C_{1-6}alkyl;

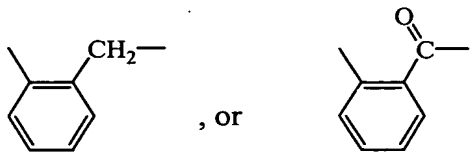
or R^9 and R^{10} taken together with the nitrogen atom to which they are attached may form a pyrrolidinyl, piperidinyl, homopiperidinyl, piperazinyl, or morpholinyl group, optionally substituted with C_{1-4}alkyl or C_{1-4}alkyloxy; and

Q is a bivalent radical of formula

$-CH_2-CH_2-$	(e-1),	$-CO-CH_2-$	(e-6),
$-CH_2-CH_2-CH_2-$	(e-2),	$-(CH_2)_2-CO-$	(e-7),
$-CH_2-CH_2-CH_2-CH_2-$	(e-3),	$-CO-(CH_2)_2-$	(e-8),
$-CH=CH-$	(e-4),	$-CO-CH_2-CO-$.	(e-9),
$-CH_2-CO-$	(e-5),	$-CH_2-CO-CH_2-$	(e-10),

wherein optionally one or two hydrogen atoms on the same or a different carbon atom may be replaced by C_{1-4}alkyl, hydroxy or phenyl, or

Q is a bivalent radical of formula



(e-11) , or (e-12)

2. A compound as claimed in claim 1 wherein R^5 is a radical of formula (d-1) wherein X is oxygen, and Q is a radical of formula (e-1) or (e-2).

3. A compound as claimed in claim 1 R^4 is hydrogen; $-Z^1-Z^2-$ is of formula $-CH_2-CH_2-$ (a-4), Alk is $-CH_2-$; the bivalent radical —(A)— is of formula (c-1) wherein R^{11} is hydroxy or methoxy and m = 0; and R^5 is a radical of formula (d-1) wherein X is oxygen, R^7 is hydrogen, and Q is (e-2).

4. A compound according to claim 1 wherein R^4 is hydrogen; $-Z^1-Z^2-$ is of formula $-CH_2-CH_2-$ (a-4), Alk is $-CH_2-$; the bivalent radical —(A)— is of formula (c-2) and m = 0; and R^5 is a radical of formula (d-1) wherein X is oxygen, R^7 is hydrogen, and Q is (e-2).

5. A compound according to claim 1 wherein R^4 is hydrogen; $-Z^1-Z^2-$ is of formula $-CH_2-CH_2-$ (a-4), Alk is $-CH(OH)-CH_2-$; the bivalent radical —(A)— is of formula (c-1), m = 0, R^6 is hydroxy or hydroxymethyl; and R^5 is a radical of formula (d-1) wherein X is oxygen, R^7 is hydrogen, and Q is (e-2).

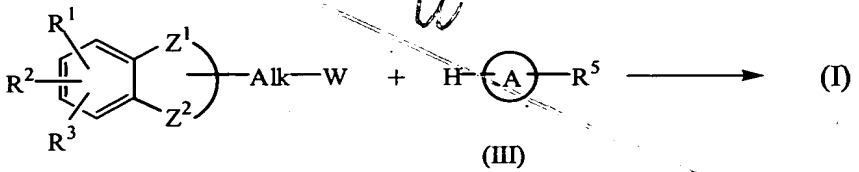
6. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically active amount of a compound as claimed in any of claims 1 to 5.

7. A process for preparing a pharmaceutical composition as claimed in claim 6 wherein a therapeutically active amount of a compound as claimed in any of claims 1 to 5 is intimately mixed with a pharmaceutically acceptable carrier.

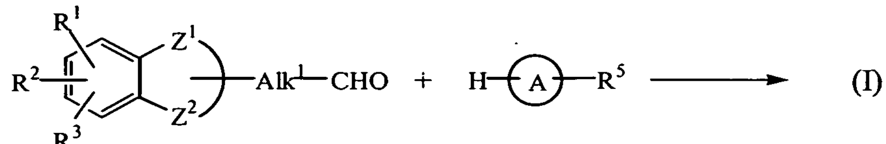
~~8. A compound as claimed in any of claims 1 to 5 for use as a medicine.~~

9. A process for preparing a compound of formula (I) wherein

a) an intermediate of formula (II) is alkylated with an intermediate of formula (III) in a reaction-inert solvent and, optionally in the presence of a suitable base,



b) an intermediate of formula (IV), wherein $Alk^{1'}$ represents a direct bond or C_{1-5}alkanediyl, is reductively alkylated with an intermediate of formula (III);



(IV) (III)

wherein in the above reaction schemes the radicals $-Z^1-Z^2-$, R^1, R^2, R^3, R^4, R^5, Alk and the bivalent radical —(A)— are as defined in claim 1 and W is an appropriate leaving group;

c) or, compounds of formula (I) are converted into each other following art-known transformation reactions; or if desired; a compound of formula (I) is converted into an acid addition salt, or conversely, an acid addition salt of a compound of formula (I) is converted into a free base form with alkali; and, if desired, preparing stereochemically isomeric forms thereof.